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H. SEIDELIN

Transactions of the 15th International Congress on Hygiene and Demography, 1912.

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THE NATURE AND CONTROL OF YELLOW FEVER

BY

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Reprinted from the Transactions of the Fifteenth International Congress on Hygiene and Demography, held at Washington, D. C., September 23–28, 1912

(171) WASHINGTON : GOVERNMENT PRINTING OFFICE : 1913

THE NATURE AND CONTROL OF YELLOW FEVER.

HARALD SEIDELIN, Liverpool, England.

Yellow fever is an infectious disease produced by *Paraplasma flavigenum* and transmitted by *S. fasciata.* The latter statement has met with universal acceptance and we may at present take its correctness for granted. But it is worth while to examine the rather elaborate structure which has been erected on this foundation. The theory, as it now stands, embraces the following particulars: Yellow fever is transmitted by *S. fasciata* and by no other means, in particular by no other mosquito. The transmission can only take place after the yellow-fever parasite has undergone a development in the mosquito, the duration of which is, approximately, 12 days. Yellow-fever blood is infectious during the first part of the disease, but not after the third day. Transmission is believed to take place at night-time only. Hereditary transmission of the yellow-fever germ from mosquitoes to their offspring and infection of one mosquito from another, without the intervention of a human host, are generally considered as unproved possibilities. Each of these points must be discussed separately.

I may say at once that conclusions on these secondary points have not been drawn by the United States Army Commission. Reed and his fellow workers were very careful in their statements; but the assertions of later observers have been repeated so often that they are now almost universally believed.

The axiom that yellow fever is transmitted by no other mosquito than *S. fasciata* is an assertion entirely without proof. It is nevertheless now repeated in most textbooks and even in special literature dealing with yellow fever. In fact, no experiments have ever been made with stegomyia species other than *S. fasciata.* In trypanosome infections, in malaria, and in babesia infections, we know that insects belonging to different species, to different genera, even, may serve as transmitters. We should be careful in drawing conclusions on yellow fever with the very scarce material at hand.

That yellow fever is transmitted in nature by no other means than by mosquitoes has never been proved, but is extremely probable in view of our knowledge of protozoal diseases.

The yellow-fever germ is supposed to undergo a development in the mosquito of 12 days' duration. This is made probable by the

negative results of experiments in which a period of less than 12 days had elapsed after the mosquito had sucked blood from an infected patient until it was allowed to bite a nonimmune individual. This theory corresponds well to the observations of Carter and others on the extrinsic incubation period, and is likely to be correct; but it can not be considered conclusively proved, as the negative experiments referred to were not numerous and, on the other hand, there is a comparatively large number of negative results in cases in which all conditions for obtaining positive results were fulfilled.

Yellow-fever blood is considered infectious during the first three days of the disease only, but on very scanty evidence, as I have previously pointed out. My argument has been objected to, but not shown to be erroneous, and I must again assert emphatically that we here have to do with a theory which is sorely deprived of foundation. The negative experiments of the Army commission prove nothing in this respect. In Carroll's table of 22 cases, with 32 negative inoculations, we find two inoculations only in which the patient bitten was in a later period than the third day, while the interval allowed in the mosquito was more than 12 days (13 and 14, respectively). In 10 inoculations both conditions for favorable results were fulfilled (patient bitten during first three days of disease and intervening period in mosquito 12 days or more). In the remaining 20 inoculations the interval in the mosquito was less than 12 days, which circumstance alone would explain the negative result. It really surprises me that anybody can take this table as an argument in favor of the three days' infectiousness.

The responsibility for this dogma rests with Marchoux and Simond, and theirs should be the honor for having pronounced it, should it finally prove to be correct, but proved it they have not. I have in a former paper analyzed the four experiments, which sustain their argument, and shall not go into details here. The experiments are both very few and of very relative value.

Transmission of yellow fever is said to take place only during the night. This doctrine is supported by a considerable amount of epidemiological evidence, mostly from the premosquito period. The general knowledge of *S. fasciata's* biology did not seem at first to answer the epidemiological experience, as it is almost universally recognized that *S. fasciata* bites indifferently at day and at night, or it is simply called by several authors a day mosquito, thus differentiating it from the typical night mosquito. The apparent contradiction between these experiences has, however, been explained by Marchoux and Simond, who found that only young females, which suck blood for the first time and have consequently no chance of being previously infected, bite at daytime, while the older and possibly infected females have learned cautiousness and remain hidden

during the day, to sally forth to attack in the darkness. If this holds good the old observation need not surprise us, but I do not think the question can be looked upon as finally settled. Severe mistakes might occasionally occur if nonimmunes were taught that they could during the day visit yellow-fever infected places with absolute safety. The matter is evidently of very great practical importance for foreigners, residents, and visitors in yellow-fever countries.

Hereditary transmission in mosquitoes and infection of mosquitoes by feeding on sugar water containing triturated infected mosquitoes have been observed by Marchoux and Simond in one experiment of each kind. The latter mode of transmission would probably be of quite exceptional occurrence in nature, but the former might explain some obscure epidemiological facts especially the apparently spontaneous, isolated outbreaks in sparsely populated countries.

With regard to the pathogenic organism in yellow fever I shall not discuss earlier investigations, as I have done so in another paper. I shall only refer to my own investigations, which took their beginning in 1908, and of which I published a preliminary note in 1909 and later on more detailed accounts. The limited time at my disposal does not allow me to enter into detailed descriptions, but I would briefly refer to the results obtained on the expedition to Yucatan for the Liverpool School of Tropical Medicine, from which I have just returned. The detailed report of this expedition will appear in a few weeks.

The parasite for which I have proposed the name of *Paraplasma flavigenum* has been found by me in earlier researches in over 90 cases of yellow fever out of a little more than 100 cases examined, and, in the last series, in 16 cases out of 17 cases officially diagnosed, clinically or post-mortem. Moreover, *P. flavigenum* was found in 21 cases not officially confirmed as yellow fever, but many of them clinically very much suspected of being so, and in none could this diagnosis be excluded. The diagnoses given in these cases were mostly gastric fever, bilious fever, or similar. Finally, the same intracorpuscular parasite-looking bodies were observed in two apparently healthy native children. These two cases, together with two similar ones which I have observed during my earlier investigations, may represent very mild infections, or the individuals may be chronic parasite carriers. A very large control material, consisting of over 400 cases, mostly of febrile diseases, as malaria, typhoid fever, etc., were carefully examined with negative results.

P. flavigenum has been observed from the first to the fourteenth day of the disease. There is no reason, however, to consider 14 days as a general time limit for its presence, as the corresponding case was a very prolonged one, with a pronounced recrudescence after 5

or 6 days. That the parasite has been found on the tenth day in a very mild case represents, relatively, a later stage of the disease.

The parasite is morphologically polymorph. The forms most commonly observed are small, intracorpuscular, consisting of one or two chromatin granules, and a more or less well-defined protoplasmic body. The largest intracorpuscular elements have been seen in smears from liver and spleen. Free elements have been seen, both in smears and in organs.

Many of the intracorpuscular elements are not unlike forms of babesia; others are more similar to theileria, and others to anaplasma. It has, therefore, been proposed to establish a new genus, paraplasma, in the family Babesiidæ.

The parasites stain, with some slight difficulty, with Giemsa's stain, and according to other modifications of Romanowsky's method; but in all cases staining should take place for a somewhat longer time than in the case of malarial parasites. It was an agreeable surprise that good results were obtained with Giemsa's quick method, prolonging the action of the undiluted stain to 1 minute, and of the diluted to 10 minutes, instead of half a minute and 5 minutes, respectively. Satisfactory results have also been obtained with various hematoxylin methods, especially with Delafield's solution and with Heidenhain's iron-hematoxylin, as well as with my own iron-hematein technique. The latter group of methods are particularly useful in staining sections, but are also of use in checking the results obtained with the Romanowsky method. There is at present a tendency to regard Giemsa's and other azur-eosin stains as particularly unreliable, a somewhat exaggerated tendency, I believe, but, of course, it is always a safeguard to use several methods.

Before we discuss the measures to be taken against yellow fever a few words should be said with regard to its epidemiology.

It was believed, when it was found that yellow fever is transmitted by mosquitoes, that it would only be a question of a few years to stamp it out. Now this has not been the case. It is not, however, the place here to inquire in detail why this has not been possible, but it appears that the success of the campaign in some places, and its failure in others, have supplied a remarkable proof of the correctness of the mosquito theory; mosquito extermination has been comparatively easy in large cities and in limited districts under the direct control of a powerful government, and it is in such places only, as Habana, New Orleans, Panama Canal Zone, Rio de Janeiro, and Vera Cruz that really demonstrative results have been obtained. Not in all of these places has the number of mosquitoes been kept continually at a very low level; in Habana I have been informed that mosquitos, including *Stegomyia fasciata*, have lately become more common than in previous years, and some authorities have told me

that they were not at all uncommon in the Canal Zone. This should not be so; the careful vigilance should be kept up, as long as there is any possibility of reintroduction of infection. This possibility not only exists, but is abundantly present. We should be cautious and not feel secure too early; the history of epidemics teaches the lesson that the great infectious diseases are subject to oscillations, on which even the most radical measures have little influence.

To give an idea of the actual prevalence of yellow fever, I shall only mention that 716 deaths were officially reported in 1910 and 488 in 1911; in the first six months of 1912 there have already been about 500 deaths. There is little doubt that these figures represent a minimum. In the Yellow Fever Bureau Bulletin we completely abstain from summing up the cases reported, as it is common knowledge that the reports of cases are much more incomplete than those of deaths. and from some places the reports give only the number of deaths. If we calculate a mortality of about 20 per cent, then there would have occurred about 2,000 cases of yellow fever in the first six months of this year. This figure would include only comparatively typical cases which could be recognized clinically without much difficulty; if quite mild and atypical cases were included, the mortality would probably not attain 20 per cent.

One of the most important points in the epidemiology of yellow fever is the existence of unrecognized and unrecognizable cases. It is the experience of nearly all observers that yellow fever may present all degrees of intensity from severe, fatal cases to mild, atypical attacks of very short duration.

Cases belonging to the second group are not uncommon. Their importance for epidemiological questions is obvious. It is asserted by both ancient and modern observers that the susceptibility of an individual diminishes with the length of time during which he has resided in a yellow-fever-infected country. This phenomenon we are entirely unable to explain, if we do not admit that the (relative or absolute) immunity has developed as a consequence of acquired infection.

This matter is very clear, and will be universally agreed to, I believe, as long as we deal with foreigners. But when the same consideration is extended to natives opposition is often met with. Nothing, however, can be more clear. If an individual is immune to yellow fever, it is reasonable to conclude that he has already gone through at least one attack of the disease.

When the immunity is considered in this way, we can form a definite idea of epidemiology. Yellow fever is endemic in certain areas, at present in several parts of Mexico, Brazil, Central America, and Ecuador, and in the Old World in West Africa. The infection is continuously maintained in a mild form in those countries, but

tends to give rise to epidemic outbreaks on some occasion or other; for instance, the arrival of a considerable number of nonimmune foreigners. In the meantime, between outbreaks the infection is continued in natives who are infected in childhood, and therefore not liable to typical attacks later on. Most cases in native children are atypical and many are mild. They are consequently not recognized, but nevertheless confer a certain degree of immunity. Later in life these individuals will be exposed continually to mosquito bites and probably be bitten many times by infected *S. fasciata.* They will not, however, develop yellow fever, but either present no symptoms at all or only those of a mild febrile disorder. In the former case we would have to speak of microbe carriers; in the latter simply of mild infections. It is very likely that microbe carriers exist, but we have no idea for how long a time parasites may remain living in their blood. Minchin advocates the view that the existence of microbe carriers—i. e., symbiosis—demonstrates a higher degree of adaptation to the host than an infection which does harm to or even kills the host. In yellow fever a very well-advanced stage of adaptation seems to exist. Thus we may expect to find chronic carriers of yellow-fever microbes.

This hypothesis goes a long way to explain many epidemiological facts which remain obscure at present, especially the occurrence of repeated but separate outbreaks in sparsely populated areas (Sudan), where not even the existence of unrecognized cases with mistaken diagnosis would furnish a sufficient explanation of the persistence of the virus in the area.

Severe, even fatal, cases of yellow fever are occasionally observed in natives in endemically infected countries. The apparent contradiction between this fact and the ordinary immunity of natives may probably be explained in the following way: The large majority of natives in all places of an endemically infected country, and in populated centers practically all natives, have for centuries become infected with yellow-fever virus, each individual repeatedly, even frequently, during his lifetime. Thus a continuous supply of virus is kept up, and all individuals are continually exposed to infection. In the case of foreigners arriving at such a place the result is that all are inoculated with the germ, and a certain percentage taken ill with typical symptoms, whilst others develop mild, unrecognized infections, and others again are quite slowly vaccinated without ever presenting pathological symptoms. Briefly we have similar differences in susceptibility as in other infectious diseases. In the natives conditions are different. They are all infected in childhood, and in this case two circumstances may concur to modify the result of an inoculation. Firstly, cases of yellow fever in childhood are often quite different from those observed in adults, a circumstance which may

not influence the prognosis, but cause the disease to be called by other names. Secondly, a certain degree of immunity may have been transmitted hereditarily, antibodies having passed from mother to child; this factor would influence both prognosis and diagnosis. A few cases in native children might be both typical and fatal—that is what occurs even in large, severely infected cities—but to the rule that all children become inoculated there would be no exception. Therefore, there are no cases of severe yellow fever in adult natives in infected cities. In country districts conditions are somewhat different. Not only the number of human hosts is less, but in many cases also that of the mosquito hosts, other mosquitos taking to a certain extent the place of *S. fasciata*. Thus, it may happen in a district that the virus dies out, and, if communication is scarce, and especially if people never spend the night—the most dangerous time for infection—away from their districts, then a generation may grow up, the members of which have not acquired immunity, and have soon lost their hereditary immunity. In the case, then, that the virus is reintroduced into such a community, infection will spread and kill as it is apt to do in a country where *S. fasciata* prevails but which has hitherto been exempt from infection.

It is evident that, if so many varieties of yellow fever exist, the diagnosis must be one of extreme difficulty. And nothing can be more important for a successful campaign against yellow fever—in exposed and recently infected areas—than an early and indisputable diagnosis. A few observers (Guiteras and Lebredo) assert that an indisputable, if not early, diagnosis can be made in all cases of yellow fever, but most authors as well as most experienced practitioners whom I have met with regard this as an impossibility. Not a single symptom is constant nor pathognomonic. The relative intensity of the symptoms varies considerably. One can not lay too much stress on a careful clinical examination, but I must emphasize that I now consider an examination of the blood necessary not only to exclude a diagnosis of malaria but also to demonstrate the existence of the yellow-fever germ. Malaria can not always be excluded because of the absence of malarial parasites, namely, if quinine has been taken, and, on the other hand, the presence of Plasmodium does not exclude the diagnosis of yellow fever, as the two diseases may well exist at the same time. The demonstration of *P. flavigenum* has in several cases enabled me to make a diagnosis of yellow fever before seeing the patient, and the diagnosis has afterwards been confirmed clinically. The demonstration of *P. flavigenum* is difficult; a very thorough examination of well-prepared and intensely stained blood smears is necessary, and the best microscopic outfit is none too good. It is almost useless to work with an ordinary twelfth-inch immersion lens. I have often seen the parasites with such a lens when I was

aware of their existence and had localized them before, but for the detection of paraplasma I consider an apochromatic immersion lens in perfect shape and compensating oculars a necessity. The examination should be repeated if a negative result is obtained and the case continues suspicious. My belief is that this means of diagnosis will become as essential in yellow fever as is the bacteriological examination in plague and cholera. There may be the additional comparison with the conditions in cholera that not only persons actually suffering from yellow fever may thus be detected, but also microbe carriers. This would, of course, be a considerable advance from an epidemiological point of view.

Prophylactic measures may be divided into two groups, one dealing with the protection of mosquitoes against acquiring infection from human individuals and the other with the protection of non-immunes against the bites of infected mosquitoes. The former group includes the detection of infected individuals and their isolation, the second of segregation and mosquito protection. Mosquito-destroying measures are common to both groups and may be first considered.

We destroy mosquitoes by killing larvæ or impeding the laying of eggs and by killing adult mosquitoes. For the former purpose we have to abolish unnecessary water containers and to screen or oil such containers which can not be dispensed with, or, in some cases, to stock them with larva-eating fish. I have failed to see the advantage of substituting the use of chemical poisons dissolving in water for the generally accepted method of spreading petroleum on the surface of the water; the latter method seems to me the least objectionable. It is unnecessary to enter into a detailed discussion of larva-destroying measures; those in general use are efficient if carried out thoroughly. Unfortunately the position regarding the destruction of adult mosquitoes is not so well defined. So far fumigation with sulphur is the method in general use; it is an efficient and comparatively cheap method, but the disagreeable smell and the damage done to metals, fruit, and vegetables is a serious drawback.

The Nocht-Giemsa method, disinfection with CO, which is recommended for the destruction of rats, is said to be inefficient against mosquitoes. I have, however, found coal gas to be a powerful culicide in laboratory experiments, but have so far made only a few experiments on a larger scale, of which the result seems to be that it is quite feasible to obtain good results in this way. The action of the gas must be somewhat more prolonged than that of the sulphur dioxide, but the cost was not considerably higher, not even in Yucatan, where gas is very expensive. As far as I can judge, the recently published fumigation with cresyl (Bouet and Roubaud)

would seem even more efficient and cheaper than both the sulphur and the gas methods, without possessing serious inconveniences, and I am therefore at present engaged in a study of its practical application. The pyrethrum method is not quite reliable, as the mosquitoes become stupified only but are not killed, and cyanide and phenol camphor are somewhat expensive.

The measures which have for their object to impede mosquitoes of gaining access to infected individuals, namely, early detection of cases and their isolation, are of the utmost importance as protection measures against the introduction of yellow fever into noninfected places, in which *S. fasciata* are present, but of much less importance in endemically infected areas. They make it necessary to carry out a careful inspection of all passengers arriving from infected places and their observation during the possible incubation period, either in quarantine or by daily inspection.

The protection of nonimmunes against the bites of infected mosquitoes must practically consist in their thorough protection against mosquito bites in general, at any rate during night, as it is the only safe plan in endemic areas to regard all stegomyiæ as infected, and as, in such areas, a very high percentage of mosquitoes are stegomyiæ, which occur together with other mosquitoes. Segregation, living at a distance from the native quarters, can, of course, in some places be useful to a certain extent, but it is by no means an efficient measure. And to pass one's whole time in a screened house or, at any rate, each night from 4 or 5 o'clock in the afternoon to 8 in the morning is a way of living which will soon become insupportable to most people. Therefore, protection of nonimmunes in endemic areas is theoretically a very valuable measure, but practically it is always carried out in a very imperfect way and can not be relied upon.

In order to put matters clear and as a basis for discussion I shall now briefly sum up the measures which I think should be put in force in each of the following three cases: (1) Endemic areas, (2) exposed places, and (3) epidemics in places where yellow fever is ordinarily absent.

Endemically infected places.—In these places all stress should be laid on the eradication of mosquitoes, and as the destruction of adult mosquitoes on a large scale in a whole city is utterly impracticable it follows that all available energy should be directed toward the destruction of larvæ or toward the prevention of mosquitoes depositing their eggs, the previously mentioned measures being carried out officially.

No measures need be taken in the case of running water, but it can not be taken for granted that mosquito larvæ do not thrive in water because it is frequently moved, if it is, on the other hand, left stagnant for a considerable length of time. Thus, larvæ have been

found in wells from which water used to be extracted several times a day with a bucket. Also containers which are said to be emptied daily should be looked upon as suspicious. They contain frequently larvæ, which go to the bottom when the container is emptied and remain living in a very small quantity of water until the container is filled again.

These measures can be made obligatory for householders and can be enforced by fines, or they can be carried out by the health authorities. The latter is, I believe, the better plan.

In either case, frequent inspections are necessary in order to make sure of the absence of forbidden collections of water and that oiling and screening are properly carried out. In the case of cesspits it must be remembered that mosquitoes may enter and escape through a pipe outlet, even if several meters long.

These are the principal measures in endemic areas and should, if faithfully carried out, lead to the complete eradication of mosquitoes. Additional measures may be useful, as the detection of cases, their isolation, and fumigation of infected houses; but their importance can not be very great, considering that for each case of typical yellow fever, which always occurs in a foreigner, there are probably tens and very likely hundreds of cases, mostly in natives, which are never detected. Therefore, if the funds available are not unlimited, as they seldom are, it will be more useful to employ all the forces to destroy mosquitoes, and simply exact from practitioners' reports of all suspicious cases, instead of keeping up a costly system of inspectors to visit the residences of foreigners and occasionally detect a case on the third or fourth day of yellow fever, sometimes later, but very seldom before, and often not at all.

Exposed places should also rid themselves of mosquitoes, so that there would be no danger of spreading should a case of yellow fever happen to be introduced. An exposed place is one where *S. fasciata* is present, and the risk incurred by the introduction of yellow-fever cases increases proportionately to the prevalence of stegomyiæ. If these mosquitoes are completely exterminated the place ceases to be exposed to infection and there need be no measures against the import of cases. But as long as this is not attained the greatest possible care should be taken to avoid introduction of individuals suffering from yellow fever. And in all places where the temperature conditions are favorable for *S. fasciata*, the import of mosquitoes should be prevented by all means.

Antimosquito quarantine consists in careful fumigation of all ships arriving from infected or suspected ports, unless it can be reasonably proved that a ship has not been exposed to the introduction of mosquitoes on board in such a port. As proof of this a certificate might be accepted stating that the ship has remained moored

during the whole of its stay at a safe distance, i. e., from 200 to 500 meters, according to the conditions of the harbor, whether open and exposed to wind or closed. For loading and unloading mosquito-proof lighters must have been employed. In the case of screened ships the exemption may be made that it should form no objection that they had been close to the shore or even at a pier, in order to take passengers on board, if all nonscreened compartments, particularly the holds, have been kept carefully closed during that time.

Fumigation should include all parts of the ship. Under no conditions should the holds be exempted, particularly in fruit ships, which are more likely to harbor mosquitoes than any other.

With regard to passengers, they should pass an initial examination, state their point of destination, and sign a declaration that they will report to the local health officer twice daily for two weeks. In the event of any suspicious sign they would be immediately isolated. Passengers arriving in mosquito-proof ships, but not in other ships, might have the number of days since the departure from an infected port discounted from the total of 14.

Several authorities maintain that this observation of passengers is insufficient and advocate the real quarantine system. But when it is considered that Germany, with a large land frontier and immense traffic, has been able to protect herself against importation of cholera from Russia for years, it seems strange that more stringent measures should be necessary in the case of the comparatively limited maritime traffic from yellow-fever places to neighboring ports. Another point of importance is also that it presents little difficulty to extend the observation period to a fortnight instead of six days, but it would be nearly impossible to establish a quarantine of 14 days, which must be considered necessary in view of the experience of Marchoux and Simond, that a natural incubation period of 13 days is occasionally observed.

An additional and very important advantage is that this system can be easily applied to all passengers, immunes and nonimmunes. Health authorities are thus saved the discussion of doubtful cases of immunity and the possibility of repeated infections is taken into account.

Thus mosquito-proof ships should have their screened departments exempted from fumigation and their passengers should be allowed a shorter observation period corresponding to the duration of the voyage; other ships should be completely fumigated and their passengers should complete the whole period of observation. A careful mosquito inspection should always be made on screened ships before any exemption is conceded.

In the case of an epidemic outbreak in a nonendemic area the importance of measures is inverted as compared with the conditions

in endemic areas. Larvæ destruction and prevention of mosquito breeding take a secondary place; detection of cases, isolation, and fumigation of infected houses, on the other hand, become the principal measures.

Finally, a small number of nonimmunes on expeditions, and in similar cases, should protect themselves as far as possible by segregation and screening.

I believe that the individualizing methods here advocated would be more efficient and cheaper as well as less oppressive than the combined and often more stringent methods which are in use in some places.

There is no time left to discuss classification of ships; I shall only say that in my opinion there is no reason to distinguish between infected and suspected ships; a ship with yellow-fever cases on board constitutes no danger per se; on the other hand, a ship carrying mosquitoes, but with no yellow-fever cases, may be extremely dangerous. It is unjustifiable to declare a ship indemne after 20 days (extrinsic and intrinsic incubation), as there is no guarantee that mosquitoes would always infect individuals on their first day on board, instead of later on; nor can the possibility be excluded that they might remain in the hold during the passage and escape on arrival.

DISCUSSION.

Col. L. M. Maus, Medical Corps, United States Army, chief surgeon eastern division, in his discussion of Surg. White's paper, stated that the crusade against yellow fever was successfully carried out by means of screening with 18-inch mesh and destruction of the larvæ. The troops at Jackson Barracks, that city, were kept in the garrison under quarantine and the post newly screened. Although surrounded by many cases of yellow fever in adjoining city blocks, no case occurred among the troops. Yellow fever moves regularly from house to house, which proves that the stegomyia travels very slowly. During the epidemic in Jacksonville, Fla., in 1877 the physicians noticed this fact, but did not understand the reason. It is possible that the neighbors next door visited the house infected and thus got the disease and transferred it along.

Dr. Eduardo Licéaga, president Superior Board of Health, Mexico: Knowing what are the three requisites for the propagation of yellow fever, to wit, a person suffering of the disease, the transmission of the cause through the bite of the mosquito, and a nonimmune bitten, we found that the disassociation of the three was enough to avert the spread of the disease. The easiest one to disassociate was the patient himself, whom we protected from being bitten by the mosquitoes by isolating him in a room protected with wire screens.

With only this method we succeeded in reducing greatly and finally making the disease disappear from all cities and places except

Yucatan, where, due to the existence of unrecognized and unrecognizable cases, we have been and are fighting the mosquitoes themselves by cleaning all pools and stagnant waters and by preserving all water deposits free from larvæ by visiting each dwelling house every 12 days to see that all water deposits are kept free from larvæ.

With this method, together with the isolation of the patient and fumigation of every place where a case occurs, we have stamped out the yellow fever from every place in Mexico, except Yuzatan, and from this place it is now rapidly disappearing.

Capt. CHARLES F. CRAIG, Medical Corps, United States Army: I have been much interested in following Dr. Seidelin's work upon his so-called parasite and yellow fever. I have read his publications, and while I have not seen his preparations I have seen his drawings, and presuming that they are accurate representations of the preparations, I must say that I do not believe the objects pictured are parasites. I have had over 12 years of experience with the Romanowsky stains, as Leishman's, Giemsa's, Wright's, and others, in blood work, and I know that they are full of pitfalls, and preparations stained with them often present appearances in the red corpuscles resembling parasitic bodies. It is therefore necessary to be exceedingly careful in drawing conclusions regarding a supposed parasite stained in blood with these methods. Personally, I believe that Dr. Seidelin's bodies are probably artefacts or due to degenerative conditions in the blood corpuscles, for I have seen similar bodies in the blood of patients suffering from other diseases, especially malaria.

I must take exception to Dr. Seidelin's statement that it is impossible to reduce the number of mosquitoes to a noninfective minimum in cities where yellow fever is endemic. This has been done in Habana, Rio Janeiro, and the Canal Zone, as we all know.

Regarding other statements in the paper, tending to throw discredit upon the results of the Yellow Fever Board, headed by Walter Reed, I would only say that in the fact that this dread disease has disappeared wherever prophylactic measures based upon the results of this board have been enforced, we have an unanswerable proof of the truth of their conclusions.

A. J. ORENSTEIN, Canal Zone: I wish to add to what Capt. Craig said in reference to the possibility of reducing *S. calopus* to a noninfective number. It was done in Panama. Although from time to time a few *S. calopus* can be found here and there, the accidental introduction of a yellow-fever case into the city of Panama has not resulted in a secondary case. This, I think, proves conclusively that at least at the time this case was introduced the *S. calopus* were not sufficiently numerous to give rise to secondary cases.

I say this especially because of Dr. Seidelin's statement that he has been informed that *S. calopus* are not at all uncommon in the Canal Zone.

Prof. CREIGHTON WELLMAN, New Orleans, La.: I wish to state that if Dr. Seidelin's informant reported for the period I was in the Canal Zone he was mistaken in his facts. While I was in the Canal Zone I sought diligently for stegomyia, and, although an experienced collector, I found neither larvæ nor adults and indeed no other species, although such undoubtedly exist in rural districts.

Dr. H. SEIDELIN, Liverpool, England: To Dr. White I would say that it is very far from being an impossibility to screen ships—in fact, English shipowners have carried this measure into practice. One firm, the Booth Steamship Co., of Liverpool, first tried the system, as recommended by Dr. Melville-Davison, their medical superintendent, on a single ship, which went far up the Amazon and one of its tributaries. After the ship had made two such voyages without a single case of malaria or yellow fever, a thing which had not been accomplished before in their experience, they screened all their ships, I believe over 40. Practical people would not go to this very large expenditure, representing thousands of pounds, if they did not find it practicable. (Results published by Melville-Davison in Yellow Fever Bureau Bulletin, 1911, I, 6.)

To Dr. Orenstein I can only say that the information referred to was received from a prominent American health official in the Panama Canal Zone, who wrote to me that they could not possibly have had any cases of yellow fever in the zone, as the disease would then certainly have spread, since they had quite a number of stegomyia.

Capt. Craig and Dr. White seem to have misunderstood what I said about the destruction of adult mosquitoes. I have never said that they could not and should not be destroyed in the case of an epidemic; of course they should. But I have said, and I repeat it, that destruction of adult mosquitoes is of little use in endemically infected areas, where larvæ destruction and abolishment of breeding places are the only rational measures.

Capt. Craig believes that my parasites are artefacts. He has not seen them, and I think we had better delay the discussion until he has. But I may tell him that no authority who has seen my specimens has seriously entertained that idea.

Surg. Gen. Sternberg mentioned the negative results of previous investigations. I have no other answer than this—that negative results nearly always precede a positive one. In this particular case the very great advances in staining technique and construction of microscopes may have helped me to obtain better results than my predecessors.

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